

REMARKS

The Examiner has acknowledged the Response filed 13 September 2002, however, he indicates that the application is not in compliance with the sequence rules stating that the Applicants failed to amend the Specification to identify all applicable sequences by their identification numbers. Applicants have amended the Specification to identify each sequence by its sequence identification number. No new matter has been added with the amendment. Support for the amendment can be found throughout the Specification.

In addition to the amendments to the Specification, claims 74, 78, 81, 84, and 91 have been amended. The claims were amended to more clearly set forth what Applicants regard as the invention. No new matter has been added with the amendment. Support for the amendments can be found throughout the Specification.

REJECTIONS

Rejection of Claims 74, 76-78, 80-86 and 91 under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 74, 76-78, 80-86 and 91 under 35 U.S.C. §112, second paragraph, for failing to particularly point out and distinctively claim the subject matter which Applicant regards as the invention. More specifically, a) claims 74, 76, 80, 83, 84 and 86 remain rejected over the metes and bounds of the term “whole molecule parameter”; b) claims 74 and 82 remain rejected over the term “*space filling technique*,” which the Examiner alleges is not defined by the Specification in such a way that one of ordinary skill in the art would be able to determine the metes and bounds of the claimed invention; [sic] d) claims 74, 76, and 80 remain rejected over the metes and bounds of the phrase “*determining a relationship*”; e) claim 74 remains rejected over the metes and bounds of the second peptide library arising from the limitation that the plurality of peptides are “expected” to provide an indicia of an activity based upon a relationship; f) claims 74, 76-78, 80 and 91 remain rejected over the term “*indicia*”; h) claims 77 and 78 remain rejected over how a “*range*” of “*indicia*” may be “*qualified*”; i) claim 82 remains rejected over the term “*isomers*” have a definition that is repugnant to the usual meaning of that term; j) claim 82 remains rejected over the definition of the term “*isomers*” that is defined in the specification as “*the group of compounds sharing common global characteristics*”; and k) claim 85 is rejected because the Examiner states that it is not clear if Applicant intended to recite “*whole molecule parameter*” rather than “*parameter*.” Applicants respectfully traverse these rejections.

a) With regard to the rejection of claims 74, 76, 80, 83, 84 and 86 over the metes and bounds of the term “whole molecule parameter”, Applicants direct Examiners’ attention to page 28, lines 2-6 of the Specification, which defines the term as “a value that characterizes a molecule irrespective of the arrangement of its constitutive atoms. For example, a whole molecule parameter for a peptide is one that does not depend on the order or sequence of the amino acids in the peptide.” The parameters of a whole molecule include, but are not limited to, total charge, molecular weight, isoelectric point, total dipole moment, isotropic surface area, electronic charge, and hydrophobicity. (See Specification, page 51, lines 14-16.) The metes and bounds of the a “whole molecule parameter” are defined. The claims as written meet a reasonable degree of particularity and distinctness. Withdrawal of this rejection and reconsideration of the claims are respectfully requested.

b) With regard to the rejection of claims 74 and 82 over the metes and bounds of the term "*space filling technique*," which is equivalent with "space filling design", Applicants direct the Examiner's attention to the definition that can be found on page 19, lines 32 to page 20, line 2. As explained in the Specification, a space-filling design provides a strategy for gathering data at a set of design points, such that the data gathered will efficiently represent all candidate compounds, known as the candidate space. Exemplary space-filling designs include but are not limited to full factorial designs, fractional factorial designs, maximum diversity libraries, genetic algorithms, coverage designs, spread designs, cluster based designs, Latin Hypercube Sampling, and other optimal designs (*e.g.*, D-Optimal) and the like. (See page 10, line 10-14). Space-filling design is well known to those skilled in the art. Withdrawal of this rejection and reconsideration of the claims are respectfully requested.

Applicants answer in the negative in response to the Examiner's question, "If a first library were all possible pentamers and the second library were all possible tetramers with glycine at the N-terminus, for example, would the second library have been selected based upon a space filling design?" The answer is no for three reasons: 1) a space-filling design selects a representative subset; 2) a space-filling design must efficiently represent all candidate compounds; and 3) a library makes all compounds and therefore is not a selective representation. Applicants teach a space filling design representative of the total space, not to be the total space.

d) Claims 74, 76 and 80 remain rejected over the metes and bounds of the phrase "*determining a relationship*." As explained in the Specification at page 29, line 14 to page 30, line 28, the relationship is one between the measured indicia and the parameters. This relationship may be mathematical as set forth in claims 76 and 80. Withdrawal of this rejection and reconsideration of the claims are respectfully requested.

e) The Examiner has maintained the rejection of claim 74, alleging the metes and bounds of the second peptide library are not clear because the claims recite that the plurality of second test peptides are "*expected*" to provide an indicia of an activity based upon a relationship. Claim 74 has been amended to obviate this rejection. The amended claim states that the a second peptide library is predicted based upon the relationship between the indicia of activity and the parameters that satisfy the test requirement. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

f) Examiner has maintained the rejection of claims 74, 76-78, 80, and 91 over the metes and bounds of "*indicia*." The term *indicia* is used to represent a numerical value or measured value associated with an activity of interest. See for example Figure 2, which refers to measured *indicia* "of a property of interest." Withdrawal of this rejection and reconsideration of the claims are respectfully requested.

g) [sic]

h) Examiner has maintained the rejection of claims 77 and 78 over how a "*range*" of "*indicia*" (values?) may be "*qualified*."

A range of *indicia* may be qualified based upon determined values or conditions. For instance, if the indicium of interest is the molecular weight of a peptide and the range should be between 5 and 10 kD based upon test and analysis, then the range is qualified. A range may be qualified to be within, below or above the parameter of interest. (See the Specification, page 7, lines 10-23, and page 26-27, lines 6-8.) Withdrawal of this rejection and reconsideration of the claims are respectfully requested.

i) The Examiner has maintained the rejection of claim 81 alleging the term "*isomers*" is used by the claims to mean peptides or compounds "*sharing common global characteristics*," while the art accepted meaning is compounds (peptides) "*sharing the same formula but having different properties*" thus the term "*isomers*" is repugnant to the usual meaning of that term. Applicants define the term "compounds sharing common global characteristics" as "compound isomers". Within the same paragraph of the Specification defining said term applicants refer to "compound isomers" to represent the collection of proteins sharing the same molecular formula or molecular weight. See for example, on page 46, line 6-12. Applicants have preserved the normal meaning of the term. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

k) The Examiner asks if Applicant means to recite "whole molecule parameter in claim 85. Claim 85 should read "sequence specific parameter. Applicants believe Examiner is referring to claim 86, which refers to "whole molecule parameter." Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

Rejection of Claims 74, 81, 87-90 and 94 under 35 U.S.C. §102 (b) over Tenson et al.

The Examiner has maintained the rejection of Claims 74, 81, 87- 90, and 94 under 35 U.S.C. 102(b) as being anticipated by Tenson et al., stating that Tenson et al. encompasses the “space filling design.” Applicants respectfully traverse this rejection.

Tenson et al. teaches discovery of erythromycin resistant peptides by first creating a randomly generated library of peptides. Tenson et al. further teaches random selection of a second library of peptides. In contrast, Applicants teach a first library of peptides that are selected using a space-filling design as representative of the peptide library. The second library is selected based upon a relationship between the measured (indicia) of activity of the first peptides that is correlated into a relationship with at two parameters of the first test peptides. Tenson et al. does not teach or suggest the selection of peptides by space-filling designs and a relationship of at least two parameters and an indicia of activity.

Tenson et al. teaches two random peptide libraries of the form $M(X)_{20}$ and $M(X)_4$. This random selection approach does not create a subset of representative candidates that is representative of all of the respective spaces. The 5-condon library of Tenson et al., which contains a collection of pentapeptides all having methionine at the N-terminus, covers only a particular region of pentamer space. Thus, the 5-condon library of Tenson et al. as a subset of pentamer space does not representatively cover all of pentamer space. Likewise, the 21-codon library contains only methionine at the N-terminus, regardless of the peptide length (see Figure 1, where the first residue is coded as ATG (methionine) while the remaining positions are randomized). The peptides in this library also will not be representative of all peptide space.

Both the first and second libraries of Tenson et al. were constructed to contain methionine at the N-terminal position, and thus does not constitute a space filling design as set forth in the claim. The cited art fails to disclose each and every element of claim 74 and therefore does not anticipate the invention under 35 U.S.C. § 102. See *Lindemann Maschinenfabrik GMHB v. American Hoist and Derrick Company et al.*, 221 USPQ 481 (1984). Withdrawal of this rejection and reconsideration of the claims is respectfully requested.

Rejection of Claims 74, 92, 94 and 95 under 35 U.S.C. §102 (b) over Ostrem et al.

The Examiner has maintained the rejection of Claims 74, 92, 94 and 95 under 35 U.S.C. 102(b) as being anticipated by Ostrem et al, *Biochemistry* 37:1053-1059 (1998) stating that Ostrem et al. encompasses a “*space filling design*.” The examiner states, “[w]ith regard to Ostrem et al. reference, a peptide of length of 8 amino acids reads (sequence independent parameter) and the presence of a YIR sequence (sequence dependent parameter) were determined to relate to the measured first indicia of an activity. All resynthesized peptides of the second peptide library included specific amino acid motifs (the selection of peptides as well as modified peptides including the YIR sequence was a ‘space-filling technique’ because the structures around the YIR sequence were replaced by a variety of moieties).” Applicants respectfully traverse this rejection.

All of the peptides in the first library of Ostrem et al. are eight amino acids long. This is a constant value, and is not a sequence independent parameter. Further, the first library Ostrem et al. was *all* of octapeptide space generated by combinatorial chemistry. As such it represents the complete octamer universe and does not constitute a space filling design representative of the space as claimed in the instant invention. Finally, Ostrem et al. teaches that a number of different “secondary libraries” were generated. Presumably, the one selected by the examiner was the one described on p. 1056, col 1, paragraph 1. Only a handful of modifications of this library were described, such as the C-terminal p-nitroanilide (pNA) substrates, and only two peptides were mentioned (D-Tyr-Ile-Arg-pNA and Ac-Tyr-Ile-Arg-pNA). These examples do not represent a space-filling design.

Ostrem neither teaches or suggests the selection of peptides by space-filling designs as claimed in the present invention. For lack of reciting each element of the claim, the reference fails as a proper rejection under 35 U.S.C 102 (b). *Id.* Withdrawal of this rejection and reconsideration of the claims is respectfully requested.

Claim Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected amended Claims 74-76-95 under 35 U.S.C. §112, first paragraph alleging new matter was introduced by the amendments.

More specifically, the Examiner has rejected amended claims 76 under 35 U.S.C. §112, first paragraph alleging new matter was introduced by the amendment regarding the recitation of x_{ij} as a whole molecule parameter. Applicants respectfully traverse this rejection. Original claim 76 recited the nexus of whole molecular parameters to the variable x_{ij} . The amendment to claim 74, the recitation of the descriptor of “parameter” was to more clearly and specifically point out what applicant believes to be the invention. The variable is defined and its mathematical relationship to measured first indicia of a property is found on page 30, lines 19-38. An example of the use of the relationship for predicting an estimated indicia of the property is found on page 32, lines 1-2, where the use of a whole molecular parameter is stated (molecular weight). Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

The Examiner has rejected amended Claim 81 under 35 U.S.C. §112, first paragraph, alleging lack of support for the recited “...wherein said determining first indicia step is preceded by the step of defining a first peptide library...” Applicants respectfully traverse this rejection. Applicants draw Examiner’s attention to page 26, lines 21-25, in the Specification, which states “A test requirement is determined against which the measured indicia of the property are compared. The test requirement may be determined *a priori* or it may be determined before or after operations to determine a relationship between the parameter(s) of the first test compounds and the measured indicia of the property. . . .” Thus, support for the limitation of determining first indicia preceded by defining a first test peptide library recited in claim 81. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

The Examiner has rejected amended Claim 83 under 35 U.S.C. §112, first paragraph, allegedly for deleting members of the group reciting the limitation to whole molecule parameter. Applicants respectfully traverse this rejection and direct the Examiner’s attention to page 28, lines 15-21, which list parameters that include those listed in the claim. Mere limitation of a broader, amended claim does not rise to a new matter issue. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

The Examiner has rejected amended Claim 84 allegedly for the recitation of simultaneous limitations of both whole molecular parameters and sequence specific parameters. Applicants respectfully traverse this rejection. Applicants have pointed to specific disclosure for the metes and bounds of the term whole molecular parameter (*infra*). Applicants draw Examiners attention to page 11, line 10-14 within the Specification that lists “sequence-specific parameter(s) (*e.g.* z values, isotropic surface area, electronic charge index, hydrophobicity) *of individual amino acids indexed to their relative positions in the sequence.* [emphasis added]. And finally, Applicants have pointed to recitation of the use of both parameters within the specification. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

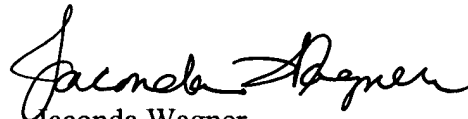
The Examiner has rejected amended Claim 74 allegedly for reciting a relationship between the first indicia of the activity and at least two other parameters, where one parameter is a whole molecule parameter and the other is a sequence specific parameter. Applicants respectfully traverse this rejection and draws the Examiners’ attention to page 12, lines 22-27, in the Specification, “. . . indicia of an activity of a plurality of test peptides from a first test peptide library are measured. A relationship is then determined between at least one parameter, preferably at least one whole molecule parameter, and the measured indicia of the activity of the test peptides. Those skilled in the art will appreciate *that the relationship may also include sequence-specific parameters in addition to a whole molecule parameter(s).*” [Emphasis added] Thus the applicants have support for the claim amendment positively reciting the relationship. Withdrawal of this rejection and reconsideration of the claim is respectfully requested.

CONCLUSION

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Jaconda Wagner (Reg. No.42,207) at the telephone number of the undersigned below. Applicants respectfully request a telephone interview with the Examiner prior to issuance of an official action on the merits in an effort to expedite prosecution in connection with the present application. Please note that this amendment follows the new proposed format and there is no marked-up version attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-1666 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,




Jaconda Wagner
Attorney for the Applicant(s)
Registration No. 42,207

Becton Dickinson and Company
1 Becton Drive
Franklin Lakes, New Jersey 07417
(201) 847-6659
66442v1

I HEREBY CERTIFY THAT THIS
CORRESPONDENCE IS BEING DEPOSITED
WITH THE UNITED STATES POSTAL SERVICE
AS FIRST CLASS MAIL IN AN ENVELOPE
ADDRESSED TO: MAIL STOP RCE,
COMMISSIONER FOR PATENTS, P.O. BOX
1450, ALEXANDRIA, VA 22313-1450
ON: JUNE 2, 2003

BY: SUSAN R. WAGNER

 6/2/03
(SIGNATURE) (DATE)